

In re Patent Application of:

**Daniell**

Serial No.: **10/520,204**

Filed: **08/26/2005**

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### **Remarks**

Applicant submits the following remarks in support of the patentability of the pending claims. With regard to the obviousness rejections, these remarks are focused on the independent claims, since if these are found patentable, so will their respective dependent claims be patentable without further consideration.

Applicant appreciates the withdrawal of the previous rejections based on anticipation of the invention by Daniell et al. (WO 01/64024), as well as those based on obviousness in view of the combined references of Daniell et al. (WO 99/10513) with Meagher et al. (US 5,965,796).

### **The Concerns Regarding Drawings, Title and Abstract**

Improved FIGS. 1A, 1B and 9 are provided. A substitute title has been submitted. A replacement Abstract is also submitted. Applicant is hopeful these replacements will be satisfactory.

### **The Objections To The Claims**

Claim 31 has been amended to obviate the Examiner's concern regarding a dependent claim being broader than its overlying independent claim.

With regard to dependent claim 9, the Examiner contends it fails to further limit the scope of claim 1. Applicant respectfully disagrees. Claim 1 recites "a transformation vector effective for stably transforming a plastid genome . . . ." Claim 9 further requires that said plastid be "selected from a chloroplast, a chromoplast, an amyloplast, a proplastide, a leucoplast and an etioplast." Even though the "selection" does not affect the structure of the genome itself, it does affect in which cellular

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organelle that genome is located. Therefore, the scope of claim 9 is substantially narrower than the scope of claim 1. Accordingly, claim 9 does in fact further limit claim 1 and should be acceptable under Section 112 interpretation.

### **The Claims Meet The Requirements Of Section 112**

Claim 36 stands rejected under Section 112 as indefinite. The Examiner contends that "it is unclear if the plastid comprises the DNA or expression cassette or if the plant cell comprises a plastid and the DNA or expression cassette."

Claim 36 is reproduced below for easy reference. A slight clarifying amendment has been made in the claim language and punctuation, which Applicant believes will obviate the Examiner's concern regarding lack of clarity.

A plant cell containing a plastid ~~including~~ which includes an expression cassette having as operably linked components[,] a promoter functional in said plastid, a *merAB* operon, a transcription termination region, a sequence encoding an antibiotic-free selectable marker, and DNA sequences flanking the expression cassette and effective for stably integrating said expression cassette into a genome of said plastid.

The Examiner also has pointed out that claim 13 is unclear. Upon review, Applicant has amended the language of claim 13 to obviate this concern; additionally, a typographical error in this claim has been corrected. The amended claim is shown below.

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The vector of claim 1, wherein said vector is stably integrated into a plastid genome and said vector is located in a single copy region of said plastid genome.

Claim 21 was also noted by the Examiner to be lacking in antecedent basis. Applicant has amended claims 20 and 21 to address this particular concern and believes these amendments obviate the rejection.

#### **The Claims Are Nonobvious Over Daniell and Rathinasabapathi**

Independent claims 1, 29, 34 and 36 stand rejected as obvious under 35 USC 103(a) over the combined references of Daniell et al. (WO01/64024) and Rathinasabapathi et al. (1994, *Planta* 193:155-162). Applicant respectfully disagrees for the following reasons.

The Examiner has recognized that the reference by Daniell et al. does not disclose BADH or an antibiotic-free selectable marker. However, the reference by Rathinasabapathi et al. is cited in combination with Daniell et al. as rendering the inventions recited in all independent claims obvious to one of ordinary skill in the art and, thus, unpatentable under Section 103(a). While Rathinasabapathi et al. teach nuclear transformation only, the reference indicates that the protein expressed is targeted to the chloroplast. Therefore, the Examiner asserts that "substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice."

Applicant points out that Rathinasabapathi et al. provide specific teachings that would guide those of ordinary skill in the art away from chloroplast transformation.

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First, Rathinasabapathi et al. caution that “although transgenic plants metabolize betaine aldehyde *at rates sufficient to confer resistance* to this compound, *their growth is still retarded* compared to controls.” Emphasis added; first page, left column, last paragraph and page 161, last paragraph, left column. It is important to note that Rathinasabapathi et al. teach that their transformed plants metabolize betaine aldehyde only at a level sufficient to confer resistance, and that the transformed plants are stunted.

Rathinasabapathi et al. additionally teach that “there was a *significant variation in BADH expression among constructions*” (emphasis added; see page 157, first paragraph below the caption “Results”); however, these data are not shown in the reference. This teaching is quite clear; significant variation in BADH expression among different constructions means no expectation of success. Keeping in mind that Rathinasabapathi et al. teach nuclear transformation, together with their warning that expression is highly variable between constructs, those skilled in the art would expect even greater uncertainties if attempting to accomplish chloroplast transformation. Accordingly, there would be no expectation of success in transforming the plastid genome. This is another teaching by Rathinasabapathi et al. that would lead the skilled away from the present invention.

Applicant submits that the expression level required to confer the ability to phytoremediate the soil within reach of the plant’s root system is much higher than the expression level necessary to confer mere resistance. The present application states that “the concept of phytoremediation [is] - using plants to remove or inactivate pollutants from soils and surface waters.” See specification at p. 2, lines 9-10. The present specification goes on to say that “no one to date has successfully transformed

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the plastid genome to express contaminant reducing proteins at levels sufficient to fully bioremediate contaminant compounds.” Page 2, lines 14-16. This assertion in the present specification, combined with Rathinasabapathi et al.’s teaching that there was significant variation in expression levels, would indicate to those of ordinary skill in the art that there would be no expectation of success in trying, first, to transform the plant’s plastid genome and, second, to obtain sufficiently high expression levels to allow for phytoremediation.

Counsel points out that Applicant has been granted previous patents related to his work in plant transformation. Additionally, Applicant has been elected Fellow of the American Association for the Advancement of Science (the AAAS). As the Examiner may know, in science this is the equivalent of an actor being not only nominated for but also elected by his/her peers to receive an Oscar®. Counsel’s point is not merely laudatory, but to emphasize that Applicant is one of extraordinary skill in the art, a recognized expert, and his statement in the application should be considered in this obviousness analysis, that “no one to date has successfully transformed the plastid genome to express contaminant reducing proteins at levels sufficient to fully bioremediate contaminant compounds.” Should the Examiner wish to have the Applicant’s declaration on file to that effect, Applicant would be pleased to provide one. The fact that no one accomplished the invention before Applicant, argues for nonobviousness.

Further support for the nonobviousness of the invention is shown by the following. The reference by Rathinasabapathi et al. was published in 1994. Applicant previously pointed out that chloroplast transformation by use of a gene gun has been known since at least about 1993 (Daniell, H. (1993) *Methods in Enzymology*, 217:536-

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556; see the previously cited reference WO 99/10513, at page 4, line 5).

Rathinasabapathi et al. could have attempted to transform plants by plastid transformation according to the technique published in Methods in Enzymology, but they did not. Further, the cited reference by Daniell and Moar (WO 01/64024) was published about 6 years after the reference by Rathinasabapathi et al. and the present application was filed 8 years after the Rathinasabapathi et al. reference became available and 2 years after Daniell and Moar. During the time following Rathinasabapathi et al., as well as the time following Daniell and Moar, no one, not one of ordinary skill nor one of extraordinary skill, arrived at the claimed invention. Only when Applicant filed the present application was the invention disclosed. This failure of the art to recognize the advantages of the present invention argues strongly for the conclusion that the claimed invention was not obvious to those of ordinary skill.

Therefore, Applicant contends that these facts indicate that one of ordinary skill in the art would not have arrived at the presently claimed invention. For those reasons, Applicant respectfully requests that the obviousness rejections of these claims based on the combined references of Daniell and Rathinasabapathi et al. be withdrawn.

Independent claims 1, 29, 34 and 36 additionally stand rejected as obvious under 35 USC 103(a) over the combined references of Daniell et al. (WO01/64024) and Meagher et al. (1999, US Patent No. 5,965,796), further in view of Rathinasabapathi et al. (1994, *Planta* 193:155-162). Applicant again respectfully disagrees.

**The Claims Are Nonobvious Over Daniell, Meagher and Rathinasabapathi**

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Independent claims 1, 29, 34 and 36 as obvious and unpatentable over Daniell et al. combined with Meagher et al. (US 5,965,796) and further in view of Rathinasabapathi et al. Applicant respectfully disagrees.

The Examiner has previously recognized that the reference by Daniell et al. does not disclose vectors containing merA or merB. The cited reference by Meagher et al., however, describes merA and merB genes but it does not teach inserting those genes into a plant together as operably-linked components in an operon. The Examiner, nevertheless, previously contended that "one of ordinary skill in the art would have been motivated to do so because expression as an operon in the plastid would allow production of stoichiometric amounts of the two enzymes in the pathway."

Applicant agrees that the Examiner has identified one of the great advantages of the presently claimed invention, but disagrees that such would have been obvious to one of ordinary skill in the art in view of the combination of cited references.

In fact, Applicant has previously argued that the cited reference by Meagher et al. is a continuation-in-part of a parent application which issued on September 16, 1997, as US Patent No. 5,668,294, titled Metal Resistance Sequences And Transgenic Plants. As indicated by its title, this parent application to the cited reference also involved transgenic plants and metal resistance, particularly mercury. As an inventor recipient of a US Patent, Meagher et al. are not of ordinary skill but are recognized as persons of extraordinary skill in the art. Yet, when Meagher et al. filed the application which resulted in the cited reference, a continuation-in-part of US Patent No. 5,668,294, they did not appreciate the advantage noted by the Examiner, that expression of the two enzymes required for mercury remediation as an operon in the plastid genome would produce stoichiometric amounts of the two enzymes in the pathway.

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Therefore, contrary to the Examiner's contention, these facts indicate that even those of extraordinary skill in the art did not recognize the advantages of the presently claimed invention, either that or, alternatively, they were unable to achieve the present invention.

Chloroplast transformation by use of a gene gun has been known since at least about 1993 (Daniell, H. (1993) *Methods in Enzymology*, 217:536-556; see cited reference WO 99/10513, at page 4, line 5). Yet, even with this information available, Meagher et al., people of extraordinary skill in the art who filed patent applications in 1995 (parent patent to the cited reference) and 1997 (the cited reference), failed to recognize or achieve the present invention, not once, but twice. Applicant believes that these facts provide strong evidence that the contention that the presently claimed invention would have been obvious is incorrect.

As shown above, the combined cited references teach the following: Daniell et al. (no teaching of merA or merB); Meagher et al. (no recognition of or teaching the advantages of inserting complete operon); and Rathinasabapathi et al. (no expectation of success in transforming the plastid genome due to significant variation in expression). Those of ordinary skill in the art would have been discouraged by these combined teachings as well as by the failure of these predecessors, people of extraordinary skill, to have achieved the stable plastid integration of a functional operon expressing sufficient levels of two enzymes required to phytoremediate mercury.

For those reasons, Applicant respectfully contends that the claimed invention would have been nonobvious to those of mere ordinary skill and requests that the obviousness rejections of these claims based on the combined references of Daniell, in view of Meagher et al., and further in view of Rathinasabapathi et al. be withdrawn.



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**Conclusion**

As set forth above, Applicant believes the pending claims are patentable over the cited art and respectfully requests such action from the Examiner.

If the further prosecution may be aided by a conference, Applicant respectfully requests that counsel be contacted at the Examiner's convenience.

Respectfully submitted,

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